```
TERMINAL (ENTER 1, 2, 3, OR ?):2

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 NEWS  3  Feb 06  Engineering Information Encompass files have new names
 NEWS  4  Feb 16  TOXLINE no longer being updated
 NEWS  5  Apr 23  Search Derwent WPINDEX by chemical structure
 NEWS  6  Apr 23  PRE-1967 REFERENCES NOW SEARCHABLE IN CAPLUS AND CA
 NEWS  7  May 07  DGENE Reload

 NEWS EXPRESS  May 23 CURRENT WINDOWS VERSION IS V6.0a,
               CURRENT MACINTOSH VERSION IS V5.0C (ENG) AND V5.0JB (JP),
               AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2001
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FILE 'HOME' ENTERED AT 20:42:33 ON 01 JUN 2001

=> file embase biosis medline caplus uspatfull

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                                                       ENTRY    SESSION
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FILE 'USPATFULL' ENTERED AT 20:43:07 ON 01 JUN 2001
CA INDEXING COPYRIGHT (C) 2001 AMERICAN CHEMICAL SOCIETY (ACS)

=> s hormone replacement therapy

L1        16113 HORMONE REPLACEMENT THERAPY
```

=> s gestagen or levonorgestrel or desogestrel or norethisterone or medroxyprogesterone or megestrol or cyproterone acetate or dienogest or drospirenone

L2 58099 GESTAGEN OR LEVONORGESTREL OR DESOGESTREL OR NORETHISTERONE OR MEDROXYPROGESTERONE OR MEGESTROL OR CYPROTERONE ACETATE OR DIENO
GEST OR DROSPIRENONE

=> s estrone sulfamate or estradiol sulfamate or estriol sulfamate

L3 77 ESTRONE SULFAMATE OR ESTRADIOL SULFAMATE OR ESTRIOL SULFAMATE

=> s l1 and l2 and l3

L4 3 L1 AND L2 AND L3

=> d l4

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 2000:98344 CAPLUS
DN 132:117958
TI Use of biogenic estrogen sulfamates for **hormone replacement therapy**
IN Elger, Walter; Lahteenmaki, Pekka; Lehtinen, Matti; Reddersen, Gudrun; Zimmermann, Holger; Oettel, Michael; Schwarz, Sigfrid
PA Jenapharm G.m.b.H & Co. K.-G., Germany
SO PCT Int. Appl., 33 pp.
CODEN: PIXXD2
DT Patent
LA German
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2000006175	A1	20000210	WO 1999-DE1496	19990513
	W: AL, AU, BA, BB, BG, BR, CA, CN, CU, CZ, EE, GE, HU, ID, IL, IS, JP, KP, KR, LC, LK, LR, LT, LV, MG, MK, MN, MX, NO, NZ, PL, RO, SG, SI, SK, SL, TR, TT, UA, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	DE 19834931	A1	20000224	DE 1998-19834931	19980728
	AU 9951481	A1	20000221	AU 1999-51481	19990513
	EP 1100509	A1	20010523	EP 1999-936276	19990513
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
	NO 2001000468	A	20010327	NO 2001-468	20010126
PRAI	DE 1998-19834931	A	19980728		
	WO 1999-DE1496	W	19990513		

RE.CNT 5
RE
(1) Elger, W; EXPERT OPINION INVEST DRUGS 1988, V7(4), P575
(2) Elger, W; JOURNAL OF STEROID BIOCHEMISTRY AND MOLECULAR BIOLOGY 1995, V55(3-4), P395 MEDLINE
(3) Leiras Oy; WO 9501161 A 1995 CAPLUS
(4) Michael, O; US 5633242 A 1997 CAPLUS
(5) Schering Ag; WO 9733589 A 1997 CAPLUS

=> d 2

L4 ANSWER 2 OF 3 USPATFULL

AN 2000:80743 USPATFULL
TI Estra-1,3,5(10)-trien derivatives, processes for their preparation and pharmaceutical compositions containing these compounds
IN Schwarz, Sigfrid, Jena, Germany, Federal Republic of
Elger, Walter, Berlin, Germany, Federal Republic of
Siemann, deceased, Hans-Joachim, late of Jena, Germany, Federal Republic
of by Christel Siemann, heir
Lucas, heir, by Margit, Mettmann, Germany, Federal Republic of
Siemann, heir, by Frank, Mitweida, Germany, Federal Republic of
Reddersen, Gudrun, Jena, Germany, Federal Republic of
Schneider, Birgitt, Jena, Germany, Federal Republic of
PA Jenapharm GmbH & Co. KG, Jena, Germany, Federal Republic of (non-U.S. corporation)
PI US 6080735 20000627
WO 9605216 19960222
AI US 1998-750943 19980202 (8)
WO 1995-DE877 19950703
19980202 PCT 371 date
19980202 PCT 102(e) date
PRAI DE 1994-4429397 19940809
DT Utility
LN.CNT 988
INCL INCLM: 514/176.000
INCLS: 514/182.000; 540/047.000; 540/113.000; 552/510.000; 552/539.000; 552/548.000; 552/552.000; 552/554.000; 552/555.000; 552/558.000; 552/610.000; 552/611.000; 552/618.000; 552/626.000; 552/650.000
NCL NCLM: 514/176.000
NCLS: 514/182.000; 540/047.000; 540/113.000; 552/510.000; 552/539.000; 552/548.000; 552/552.000; 552/554.000; 552/555.000; 552/558.000; 552/610.000; 552/611.000; 552/618.000; 552/626.000; 552/650.000
IC [7]
ICM: A61K031-58
ICS: A61K031-56; C07J043-00; C07J053-00
EXF 540/47; 540/113; 552/510; 552/539; 552/548; 552/552; 552/554; 552/555; 552/558; 552/610; 552/611; 552/618; 552/626; 552/650; 514/176; 514/182
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d 3

L4 ANSWER 3 OF 3 USPATFULL
AN 1998:1778 USPATFULL
TI Sulfamate derivatives of 1,3,5(10)-estratriene derivatives, methods for their production and pharmaceuticals containing these compounds
IN Schwarz, Sigfrid, Jena, Germany, Federal Republic of
Elger, Walter, Berlin, Germany, Federal Republic of
Reddersen, Gudrun, Jena, Germany, Federal Republic of
Schneider, Birgitt, Jena, Germany, Federal Republic of
Thieme, Ina, Graitschen, Germany, Federal Republic of
Richter, Margit, Jena, Germany, Federal Republic of
PA Jenapharm GmbH & Co. KG., Jena, Germany, Federal Republic of (non-U.S. corporation)
PI US 5705495 19980106
AI US 1996-732742 19961018 (8)
PRAI DE 1995-19540233 19951019
US 1996-17160 19960105 (60)
DT Utility
LN.CNT 495
INCL INCLM: 514/182.000
INCLS: 514/176.000; 540/113.000; 552/510.000; 552/548.000; 552/552.000; 552/558.000; 552/614.000; 552/617.000; 552/618.000; 552/624.000; 552/626.000
NCL NCLM: 514/182.000
NCLS: 514/176.000; 540/113.000; 552/510.000; 552/548.000; 552/552.000;

552/558.000; 552/614.000; 552/617.000; 552/618.000; 552/624.000;
552/626.000
IC [6]
ICM: A61K031-56
ICS: A61K031-58; C07J001-00; C07J053-00
EXF 552/510; 552/548; 552/552; 552/558; 552/614; 552/617; 552/618; 552/624;
552/626; 514/176; 514/182; 540/113
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d ab

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
AB The invention relates to the use of biogenic estrogen sulfamates for the oral discontinuous application for **hormone replacement therapy** (HRT). The discontinuous administration takes place in intervals ranging from 2 to 40 days. The invention also provides the addnl. application of **gestagens**, preferably continuously in the form of an implant or in the form of an intrauterine releasing system (IUD). **Estrone sulfamate, estradiol sulfamate**, or an N-acyl sulfamate of estrone, estradiol or estriol having up to 7 carbon atoms in the acyl chain, or a combination comprised of two or more of the active ingredients, are used as biogenic estrogen sulfamates.

=> d hist

(FILE 'HOME' ENTERED AT 20:42:33 ON 01 JUN 2001)

FILE 'EMBASE, BIOSIS, MEDLINE, CAPLUS, USPATFULL' ENTERED AT 20:43:07 ON 01 JUN 2001
L1 16113 S HORMONE REPLACEMENT THERAPY
L2 58099 S GESTAGEN OR LEVONORGESTREL OR DESOGESTREL OR NORETHISTERONE
O
L3 77 S ESTRONE SULFAMATE OR ESTRADIOL SULFAMATE OR ESTRIOL
SULFAMATE
L4 3 S L1 AND L2 AND L3

=> d 3 ab

L4 ANSWER 3 OF 3 USPATFULL
AB The invention relates to new sulfamate derivatives of 1,3,5(10)-estratriene derivatives of the general formula I ##STR1## wherein the 3-sulfamate moiety is acylated, sulfonated or amidosulfonated. Furthermore, methods for the production of the compound and pharmaceutical preparations containing this compound are described. The compounds according to the invention have an estrogenic effect.

=> d kwic

L4 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2001 ACS
TI Use of biogenic estrogen sulfamates for **hormone replacement therapy**
AB The invention relates to the use of biogenic estrogen sulfamates for the oral discontinuous application for **hormone replacement therapy** (HRT). The discontinuous administration takes place in intervals ranging from 2 to 40 days. The invention also provides the addnl. application of **gestagens**, preferably continuously in the form of an implant or in the form of an intrauterine releasing system

(IUD). **Estrone sulfamate, estradiol sulfamate**, or an N-acyl sulfamate of estrone, estradiol or estriol having up to 7 carbon atoms in the acyl chain, or. . .

ST biogenic estrogen sulfamate **hormone replacement therapy**

IT **Hormone replacement therapy**
(biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Estrogens
Progestogens
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Drug delivery systems
(implants; biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Contraceptives
(intrauterine; biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Drug delivery systems
(oral; biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Menopause
(postmenopause; biogenic estrogen sulfamates for **hormone replacement therapy**)

IT Amides, biological studies
Sulfates, biological studies
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sulfamates; biogenic estrogen sulfamates for **hormone replacement therapy**)

IT 979-32-8, Estradiol valerate
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(biogenic estrogen sulfamates for **hormone replacement therapy**)

IT 50-27-1D, Estriol, N-acylsulfamate derivs. 50-28-2D, Estradiol, N-acylsulfamate derivs. 53-16-7D, Estrone, N-acylsulfamate derivs. 68-22-4, **Norethisterone** 71-58-9, **Medroxyprogesterone** acetate 302-22-7, Chlormadinone acetate 427-51-0, **Cyproterone acetate** 797-63-7, **Levonorgestrel** 3562-63-8, **Megestrol** 54024-22-5, **Desogestrel** 65928-58-7, **Dienogest** 67392-87-4, **Drospirenone** 148672-09-7 172377-52-5 175219-34-8
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(biogenic estrogen sulfamates for **hormone replacement therapy**)

IT 50-28-2, Estradiol, biological studies 53-16-7, Estrone, biological studies 481-97-0, Estrone sulfate
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(biogenic estrogen sulfamates for **hormone replacement therapy**)

=> d 3 kwic

L4 ANSWER 3 OF 3 USPATFULL

SUMM Estrogens play a major role in hormonal contraception, in menopausal **hormone replacement therapy** (HRT), and for treating gynecologic diseases (e.g. mammary carcinoma) and andrologic diseases (e.g. prostatic carcinoma). For HRT and contraception, estrogens are mainly used together with a **gestagen**, e.g. **levonorgestrel, desogestrel, norethisterone,**

cyproterone acetate, chlormadinone acetate, **dienogest**.

SUMM . . . artificial menstrual cycle and other genital functions, which could not be done to any satisfactory extent by just using a **gestagen**. In addition, endogenous and exogenous estrogens fulfil important central nervous and metabolic functions in the female organism: normal estrogen levels. . .

DETD **Estrone sulfamate** (2.0 g) was dissolved in pyridine. Acetic anhydride (100 ml) was added to this solution, and the mixture was kept. . .

DETD **Estrone sulfamate** (1.3 g) was dissolved in a mixture of dichloromethane (45 ml) and triethyl amine (0.5 ml). p-Dimethylaminopyridine (0.455 g) and. . .

DETD Triethyl amine (0.4 ml), p-dimethylaminopyridine (0.35 g) and propionic acid anhydride (7.4 ml) were added subsequently to a solution of **estrone sulfamate** (1.0 g) in dichloromethane (35 ml). The reaction mixture was stirred for 20 hours at +23.degree. C., then it was. . .

DETD A solution of **estrone sulfamate** (2.0 g) in dichloromethane (70 ml) was esterified with butyloxylcarbonyl anhydride (2.5 g) in the presence of triethyl amine (0.8. . .

DETD A solution of **estrone sulfamate** (2.0 g) in dichloromethane (70 ml) was esterified with butyloxylcarbonyl anhydride (2.5 g) in the presence of triethyl amine (0.8. . .

```
=> s gestogen

L5         197 GESTOGEN

=> s estrogen sulfamate

L6          28 ESTROGEN SULFAMATE

=> s l1 and l5 and l6

L7           0 L1 AND L5 AND L6

=> s gestogen and hormone replacement therapy

L8          10 GESTOGEN AND HORMONE REPLACEMENT THERAPY

=> s l8 and py<1998

   2 FILES SEARCHED...
   4 FILES SEARCHED...
L9           8 L8 AND PY<1998

=> dup rem

ENTER L# LIST OR (END):l9

PROCESSING COMPLETED FOR L9
L10           6 DUP REM L9 (2 DUPLICATES REMOVED)

=> d l10 1-6 kwic ab bib


L10  ANSWER 1 OF 6  USPATFULL
PI     US 5686112  19971111                                          <--
SUMM   On the other hand, therapeutic transdermal systems in the meantime
found
       very wide application, in particular in hormone
     replacement therapy for the treatment of
       post-menopausal symptoms and osteoporosis and, with nitroglycerine, as
a
```

symptomatic treatment of angina pectoris in coronary. . .

CLM What is claimed is:
6. The molded body of claim 4, wherein said active compound comprises estrogens, **gestogens**, glucocorticoids or mixtures thereof.

AB To improve the efficacy and tolerability of customary topical applications for transdermal systemically acting pharmaceutical substances, single dosage topical pharmaceutical forms which are therapeutically exactly ready-to-administer are formed from suitable semi-solid pharmaceutical forms. The topical single doses are specified pharmaceutically with respect to their dose, their topical spreading behaviour and their permeation properties. Several of the topically ready-to-administer single doses are in this case accommodated in a common commercial packaging container. Complex treatments can be developed by means of different individual dosages or alternatively active compound combinations. As pharmacological active compounds, steroids, peptides, various analgesics, local anaesthetics and non-steroidal antirheumatics are employed in particular. The single dosage topical pharmaceutical form is a safe, easy to administer and inexpensive application form which makes possible a more exact topical therapy for systemic administrations than could previously be achieved using conventional topical administration forms.

AN 97:104144 USPATFULL|
TI Single dosage semi-solid topical pharmaceutical forms for transdermal therapy|
IN Liedtke, Rainer K., Munich, Germany, Federal Republic of
PA APL-American Pharmed Labs, Inc., West Caldwell, NJ, United States (U.S. corporation)
PI US 5686112 19971111 <--
AI US 1995-569958 19951220 (8)
RLI Continuation of Ser. No. US 1993-82939, filed on 29 Jun 1993, now abandoned
PRAI DE 1992-4223004 19920713
DT Utility|
EXNAM Primary Examiner: Page, Thurman K.; Assistant Examiner: Benston, Jr., William E.|
LREP Oblon, Spivak, McClelland, Maier & Neustadt, P.C.|
CLMN Number of Claims: 15|
ECL Exemplary Claim: 1|
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)|
LN.CNT 322|
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L10 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS
TI Severe mesenterial thrombosis can be a complication of continuously applied oestrogen and **gestogen** therapy.
SO Maturitas, (1997) Vol. 27, No. SUPPL., pp. 210.
Meeting Info.: 8th International Congress on the Menopause Sydney, Australia November 3-7, 1996
ISSN: 0378-5122.
IT Miscellaneous Descriptors
CONTINUOUS APPLICATION; ESTROGEN; FEMALE; **GESTOGEN**; GYNECOLOGY; **HORMONE REPLACEMENT THERAPY**; HORMONE-DRUG; MENOPAUSE; PATIENT; PHARMACOLOGY; SEVERE MESENTERIAL THROMBOSIS; TOXICITY; TOXICOLOGY; VASCULAR DISEASE
AN 1997:383984 BIOSIS
DN PREV199799683187
TI Severe mesenterial thrombosis can be a complication of continuously applied oestrogen and **gestogen** therapy.
AU Szendei, G. (1); Peter, A.; Magyar, Z.; Perner, F.; Papp, Z.
CS (1) Dep. Obstetrics and Gynecol., Semmelweis Med. Sch., Budapest Hungary
SO Maturitas, (1997) Vol. 27, No. SUPPL., pp. 210.
Meeting Info.: 8th International Congress on the Menopause Sydney, Australia November 3-7, 1996
ISSN: 0378-5122.
DT Conference; Abstract; Conference

LA English

L10 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2001 ACS
SO Obstet. Gynecol. (N. Y.) (**1996**), 88(6), 955-960
CODEN: OBGNAS; ISSN: 0029-7844
AB To establish whether **hormone replacement therapy** affects postural balance in postmenopausal women. Nineteen healthy postmenopausal women with vasomotor symptoms were included. Median age was 54 yr,. . . difficult tests either cancel visual and distort somatosensory inputs or give distorted information from both the visual and somatosensory systems. **Hormone replacement therapy** increased static balance performance assessed by dynamic posturog. A highly significant improvement was seen in the two most difficult tests. . . beneficial effects from estrogens on postmenopausal fracture risk may include central nervous system effects on balance. Two weeks' addn. of **gestogen** to the treatment regimen did not counteract the estrogen effects.
AB To establish whether **hormone replacement therapy** affects postural balance in postmenopausal women. Nineteen healthy postmenopausal women with vasomotor symptoms were included. Median age was 54 yr, median time since menopause was 3 yr. They underwent dynamic posturog. before and after 4 and 12 wk of transdermal estrogen treatment (17.beta.-estradiol 50 .mu.g/day) as well as after 2 addnl. weeks of combined estrogen-progestogen treatment. The dynamic posturog. method quantifies the amplitude, frequency, and pattern of body sway and tests the visual, vestibular, and somatosensory systems, which together maintain balance. The two most difficult tests either cancel visual and distort somatosensory inputs or give distorted information from both the visual and somatosensory systems. **Hormone replacement therapy** increased static balance performance assessed by dynamic posturog. A highly significant improvement was seen in the two most difficult tests between the pretreatment test and the test performed after 4 wk of estrogen therapy. This improvement was sustained after 12 wk and also during the 14th week, with the women on combined estrogen-progestogen treatment. Estrogen treatment increased balance performance measured by dynamic posturog., indicating that the beneficial effects from estrogens on postmenopausal fracture risk may include central nervous system effects on balance. Two weeks' addn. of **gestogen** to the treatment regimen did not counteract the estrogen effects.
AN 1997:28339 CAPLUS
DN 126:70344
TI Effects of hormonal replacement therapy on the postural balance among postmenopausal women
AU Hammar, Mats L.; Lindgren, Richard; Berg, Goeran E.; Moeller, Claes G.; Niklasson, Magnus K.
CS Department of Obstetrics and Gynaecology and Otolaryngology, Faculty of Health Sciences, University Hospital, Linkoping, Swed.
SO Obstet. Gynecol. (N. Y.) (**1996**), 88(6), 955-960
CODEN: OBGNAS; ISSN: 0029-7844
PB Elsevier
DT Journal
LA English

L10 ANSWER 4 OF 6 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
TI Bioavailability of orally administered sex steroids used in oral contraception and **hormone replacement therapy**
.
SO Contraception, (1996) 54/2 (59-69).
ISSN: 0010-7824 CODEN: CCPTAY
AB . . . and the various factors that may affect their bioavailability are briefly described. Information regarding the bioavailability of the estrogens and **gestogens**, some of which are prodrugs, used in

oral contraception and **hormone replacement therapy** is summarized and the implications regarding the clinical use of these steroids are discussed.

AB The concept of bioavailability is discussed with particular references to the sex steroids. Problems encountered in the measurement of bioavailability of these steroids and the various factors that may affect their bioavailability are briefly described. Information regarding the bioavailability of the estrogens and **gestogens**, some of which are prodrugs, used in oral contraception and **hormone replacement therapy** is summarized and the implications regarding the clinical use of these steroids are discussed.

AN 96237498 EMBASE

DN 1996237498

TI Bioavailability of orally administered sex steroids used in oral contraception and **hormone replacement therapy**
.

AU Fotherby K.

CS Royal Postgraduate Medical School, Ducane Road,London W12 ONN, United Kingdom

SO Contraception, (1996) 54/2 (59-69).
ISSN: 0010-7824 CODEN: CCPTAY

CY United States

DT Journal; General Review

FS 010 Obstetrics and Gynecology
037 Drug Literature Index

LA English

SL English

L10 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2001 BIOSIS

TI Bioavailability of orally administered sex steroids used in oral contraception and **hormone replacement therapy**
.

SO Contraception, (1996) Vol. 54, No. 2, pp. 50-69.
ISSN: 0010-7824.

AB. . . and the various factors that may affect their bioavailability are briefly described. Information regarding the bioavailability of the estrogens and **gestogens**, some of which are prodrugs, used in oral contraception and **hormone replacement therapy** is summarized and the implications regarding the clinical use of these steroids are discussed.

IT Miscellaneous Descriptors
BIOAVAILABILITY; CONTRACEPTIVE METHOD; ESTROGEN; FEMALE; **GESTOGEN**; GYNECOLOGY; HORMONE; **HORMONE REPLACEMENT THERAPY**; ORAL CONTRACEPTION; SEX STEROID; THERAPEUTIC METHOD

AB The concept of bioavailability is discussed with particular references to the sex steroids. Problems encountered in the measurement of bioavailability of these steroids and the various factors that may affect their bioavailability are briefly described. Information regarding the bioavailability of the estrogens and **gestogens**, some of which are prodrugs, used in oral contraception and **hormone replacement therapy** is summarized and the implications regarding the clinical use of these steroids are discussed.

AN 1996:426378 BIOSIS

DN PREV199699157434

TI Bioavailability of orally administered sex steroids used in oral contraception and **hormone replacement therapy**
.

AU Fotherby, K.

CS Royal Postgraduate Med. Sch., Ducane Road, London W12 0NN UK

SO Contraception, (1996) Vol. 54, No. 2, pp. 50-69.
ISSN: 0010-7824.

DT General Review

LA English

L10 ANSWER 6 OF 6 USPATFULL

AB The present invention provides compositions and methods for the transdermal administration of a therapeutically effective amount of a synthetic 19-nor-progesterone (ST-1435) and an estrogen, in combination, together with, optionally, a suitable permeation enhancer.

AN 94:44436 USPATFULL|
TI Transdermal formulations, methods and devices|
IN Gale, Robert M., Los Altos, CA, United States
Nedberge, Diane E., Los Altos, CA, United States
Atkinson, Linda E., Portola Valley, CA, United States
PA Alza Corporation, Palo Alto, CA, United States (U.S. corporation)
PI US 5314694 19940524 <--
AI US 1993-39593 19930326 (8)
DCD 20090616|
RLI Continuation-in-part of Ser. No. US 1992-848578, filed on 9 Mar 1992, now patented, Pat. No. US 5198223 which is a continuation-in-part of Ser. No. US 1990-605726, filed on 29 Oct 1990, now patented, Pat. No. US 5122382
DT Utility|
EXNAM Primary Examiner: Phelan, Gabrielle|
LREP Duvall, Jean M.; Sabatine, Paul L.; Stone, Steven F.|
CLMN Number of Claims: 20|
ECL Exemplary Claim: 1|
DRWN 6 Drawing Figure(s); 3 Drawing Page(s)|
LN.CNT 760|

(FILE 'HOME' ENTERED AT 20:42:33 ON 01 JUN 2001)

FILE 'EMBASE, BIOSIS, MEDLINE, CAPLUS, USPATFULL' ENTERED AT 20:43:07 ON 01 JUN 2001

L1	16113	S	HORMONE REPLACEMENT THERAPY
L2	58099	S	GESTAGEN OR LEVONORGESTREL OR DESOGESTREL OR NORETHISTERONE O
L3	77	S	ESTRONE SULFAMATE OR ESTRADIOL SULFAMATE OR ESTRIOL SULFAMATE
L4	3	S	L1 AND L2 AND L3
L5	197	S	GESTOGEN
L6	28	S	ESTROGEN SULFAMATE
L7	0	S	L1 AND L5 AND L6
L8	10	S	GESTOGEN AND HORMONE REPLACEMENT THERAPY
L9	8	S	L8 AND PY<1998
L10	6		DUP REM L9 (2 DUPLICATES REMOVED)

PI US 5314694 19940524 <--

SUMM Oral combination pills, implants and intrauterine devices for purposes of contraception and **hormone replacement therapy** (HRT) have been well documented for their problems such as inconvenience and side effects. Transdermal delivery of estrogens and progestins. . .

SUMM . . . when applied transdermally, ST-1435 does not adversely affect the serum lipid concentrations in the body. This is particularly important in **hormone replacement therapy** for treatment of estrogen deficiency.

SUMM Australian patent AU-A-15323/88 discloses a transdermal delivery system for the delivery of estrogens and synthetic **gestogens** for the treatment of climacteric syndrome (the withdrawal symptoms associated with menopause and caused by estrogen deficiency). The patent makes a general statement that natural **gestogens**, such as progesterone, do not pass through the skin in amounts sufficient to achieve adequate therapeutic effect using transdermal systems of conventional size, but that synthetic **gestogens** do have sufficient flux. Levonorgestrel (or d-norgestrel) is named in the patent as a synthetic **gestogen** which can be used in the transdermal system, and norgestrel and norethisterone-17-acetate are named as preferred synthetic **gestogens** for use in the system. ST-1435 is not mentioned as a candidate **gestogen**. It is to be noted here that a markedly greater amount of a **gestogen** and, consequently, a greater transdermal flux of the drug, is required for effective contraception than is required for treatment of climacteric syndrome. As discussed previously herein, it has been shown that levonorgestrel, the active enantiomer of the preferred **gestogen** norgestrel, does not, in fact, have a sufficient flux to provide a contraceptively effective plasma level of drug when applied. . . that the broad statement in the Australian patent is not in fact generally true and that sufficient flux of synthetic **gestogens**, particularly with respect to providing a contraceptive effect, is a continuing problem and cannot be predicted.

SUMM Thus, it is by no means obvious that a particular synthetic **gestogen** could be effectively administered transdermally, with or without a permeation enhancer, and particularly in an amount sufficient to provide a therapeutic and especially a contraceptive effect. That the **gestogen** could be delivered in a therapeutically, including a contraceptively, effective amount from a reasonably sized system is especially desired and. . .

SUMM . . . skin for a predetermined period of time the drugs and, if included, the permeation enhancer to provide effective contraception or **hormone replacement therapy**. The device is of a reasonable size useful for the application of the drugs and the enhancer to a human. . .

DETD . . . weeks, followed by application for one week of a device as disclosed herein but containing only the estrogen. For effective **hormone replacement therapy**, an alternative method of treatment is to apply devices of this invention containing estrogen only, preferably 17-.beta.-estradiol, for a period. . .

CLM What is claimed is:

11. A method for providing **hormone replacement therapy** to a woman, which method comprises: (a) administering a drug formulation comprised of 17-.beta.-estradiol and ST-1435 at a rate of. . .

13. A method for providing **hormone replacement therapy** to a woman, which method comprises the steps of: (1) administering for a period of two weeks to an area. . . fatty acids, acetylated monoglycerides, and lactylated monoglycerides, and mixtures thereof; steps (1) and (2) being repeated as necessary to provide **hormone replacement therapy**.